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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,150	07/18/2003	Anne Marie Heegaard	59573(46865)	5193

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EXAMINER	
GARVEY, TARA L	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/623,150	HEEGAARD ET AL.	
	Examiner	Art Unit	
	Tara L. Garvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 July 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/13/04, 5/18/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 9-17 are pending. Claims 1-8 were cancelled in a preliminary amendent filed on July 18, 2003.

Priority

Claims 9-17 are granted priority to provisional application 60/265,874 with a filing date of February 5, 2001.

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Denmark on 23 January 2001. It is noted, however, that applicant has not filed a certified copy of the PA 2001 00118 application as required by 35 U.S.C. 119(b).

Oath/Declaration

Applicant is now required to submit a substitute declaration or oath to correct the deficiency set forth: Claim for priority to provisional application 60/265,874 was placed under 119 (a)-(d) for foreign priority instead of 119(e) for domestic priority in the declaration.

Claim Objections

Claim 11 is objected to because of the following informalities: The osteoclast bone disease "osteolytic cancer invation" is not familiar. The word "invation" should possibly be "invasion." Appropriate correction is required.

Claims 12-14 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim is dependent from another multiple dependent claim. See MPEP § 608.01(n). In the interest of compact prosecution, claims 12-14 have been examined on the merits.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> **A person shall be entitled to a patent unless –**
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 13-15 and 17 are rejected under 35 U.S.C. 102(a) as being anticipated by Dahl et al (WO 00/24707 as referenced in the IDS submitted February 13, 2004)

Claims 13-15 and 17 are drawn to treating an osteoclast related disorder using a chloride channel blocker of the CIC family.

Dahl et al teaches a method of using chloride channel blockers that are prepared as a medicament for the treatment of osteoclast disorders (page 9, lines 10-28, page 21, lines 30-35 bridging to page 22, lines 1-10, page 23, lines 15-20 and page 38). The chloride channel inhibitors disclosed in Dahl et al have the same intended use as claimed in the instant application and therefore inherently block the same chloride channels and treat that same osteoclast related bone diseases. Thus, Dahl et al teach all that is recited in the instant claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art, relative skill in the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claim, with the most relevant discussed below.

Nature of the invention: The claims are directed to a method of using identified compounds for the treatment, prevention and alleviation of osteoclast related bone disease that are chloride channel blockers of the CIC family.

Breadth of the claim: The claims are broad in that any identified or known compound can be used to block a CIC chloride channel for treatment of any osteoclast related bone disease.

Guidance in the specification/Existence of a working example: The specification describes a screening method for identifying compounds that are potential blockers of the CIC chloride channel family. The specification indicates that any compound could be screened and that it is unpredictable which compounds that are identified will be useful as a therapeutic for osteoclast related bone disease. Furthermore, the specification does not describe any of the identified compounds or how to make any of the identified compounds.

In terms of the use of the compounds as therapeutics, the specification provides a working example for a screening method to identify compounds, but does not provide any working example or other evidence that an identified compound or blocker of CIC chloride channels are able to prevent the occurrence of an osteoclast related disease such as osteoporosis, osteolytic cancer, osteopetrosis or Paget's disease of bone in subject. Prevention requires a complete reversal of the disease state or complete inhibition of the occurrence of the disease state. *In vitro* data indicating that a compound was able to block a chloride channel does not predict the effect such a compound will have *in vivo* on the prevention of a variety of osteoclast disorders. Specifically, the specification has not taught an appropriate tested dose for each compound for each disease to be prevented in a subject, the number of times the treatment needs to be administered for each disease or the most appropriate route of administration. The lack of guidance in the specification would require trial and error experimentation to determine these factors.

State of the art/Predictability of the art: At the time of the applicants' invention, the general use of ion channel blockers in the treatment of various diseases was known. The specific use of CIC chloride channel blockers to prevent osteoclast disorders was not routine. Lark et al describes that the discovery of a role for CLC-7 chloride channel in the resorptive process in an osteoclast suggests that "CLC-7 potentially provides another excellent target for the inhibition of resorption" (Current Opinion in Pharmacology (2000), volume 2, pages 330-337, especially page 334, right column, second full paragraph). Several years after the time filing, the inventors demonstrate in an osteoporosis animal model that complete prevention of osteoporosis is not possible by treating with a chloride channel inhibitor. Schaller et al demonstrates only partial protection of bone strength and BMD with one tested compound that may be inhibiting the CIC-7 chloride channel (Schaller et al. Journal of bone and mineral research: official journal of the American Society for Bone and Mineral Research (2004), volume 19 (7), pages 1144-1153, see especially abstract and page 1151). The lack of complete prevention demonstrates that one cannot predict the ability of any of the identified compounds or known chloride blockers to completely prevent osteoporosis or any other osteoclast related bone disease.

Quantity of experimentation: In order to practice the claimed invention, one of ordinary skill in the art would have to determine how to make all the identified compounds and determine their effectiveness in prevention of a osteoclast disorder *in vivo*. The skilled artisan would not be able to use the identified compounds or other CIC blockers as a therapeutic for the prevention of osteoclast related diseases without a

large amount of trial and error experimentation to determine how to make and use the identified compounds in a treatment regimen.

Conclusion: In view of the unpredictable nature of the art, the lack of direction in the specification and the enormous amount of experimentation needed to make and use identified compounds, the experimentation would have been undue. Thus, it would require undue and unpredictable experimentation for one of skill in the art to perform the claimed invention. Therefore, the claimed invention of using an identified CIC chloride channel blocker to treat or prevent an osteoclast related disease is not considered to be fully enabled by the instant specification.

Claims 9 and 10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9 and 10 are drawn to a method of screening chemical compounds as potential therapeutics for an osteoclast related bone disease by testing the compounds on cells comprising chloride channels of CIC-3, CIC-6, CIC-7 and functional analogues thereof.

The specification does not describe all the functional analogues of the CIC-3, CIC-6 or CIC-7 chloride channels that would function in the method of screening compounds for the ability to treat, prevent or alleviate osteoclast related bone diseases.

The specification merely describes that analogues can have "substantially equivalent activity" and include splice variants, isoforms and homologues from other species. The prior art does not offset the lack of description in the specification in that it does not describe functional analogues of these CIC chloride channels that would be useful targets for compounds in the treatment, prevention or alleviation of osteoclast related bone diseases. Therefore, there is not a structural and functional basis provided by the prior art or the specification for one of skill in the art to envision all the analogues of CIC-3, CIC-6 or CIC-7 that would posses the same function. One of skill in the art would have thus reasonably concluded that the applicants were not in possession of the claimed invention for claims 9 and 10.

Claims 13 and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not describe all the compounds or all the prodrugs or products of these compounds that function as chloride channel blockers of the CIC family for an osteoclast related bone disease therapy. The specification merely describes that chloride channel blockers of the CIC family and derivatives of these compounds in the form of prodrugs can be used to treat, prevent or alleviate an osteoclast related bone disease. The prior art does not offset the lack of description in

the specification in that it does not describe all the derivatives of all the drugs that could function as a chloride channel blocker of the CIC family in the treatment of an osteoclast disorder. Therefore, there is not a structural and functional basis provided by the prior art or the specification for one of skill in the art to envision all the prodrugs or products of all the drugs that may function as a chloride channel blocker of the CIC family. One of skill in the art would have thus reasonably concluded that the applicants were not in possession of the claimed invention for claims 13 and 15.

Claims 13-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not describe any of the compounds that will be produced by the screening method for inhibitors of the CIC family or any compounds that function as chloride channel blockers of the CIC family. The specification merely describes that blockers of the CIC family of chloride channels can be used in the treatment, prevention or alleviation of an osteoclast related bone disease without describing the compounds to be used for the treatment. The prior art does not offset the lack of description in the specification in that it does not describe all the potential compounds that will be produced and used in the treatment of the osteoclast related bone disease. Therefore, there is not a structural and functional basis provided by the prior art or the specification

for one of skill in the art to envision all the compounds that would be used in the treatment of the osteoclast disorders. One of skill in the art would have thus reasonably concluded that the applicants were not in possession of the claimed invention for claims 13-17.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 13, 14 and 16 provide for the use of a blocker of a chloride channel of the CIC family, but since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 13, 14 and 16 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The metes and bounds of the claimed subject matter are not defined. It is unclear what is meant by "functional analogue" since it does not define the scope of the limitations.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. " A drug development method" is vague. What is meant by a drug development method since the limitations of the claim are already set forth in claims 9-11?

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tara L Garvey whose telephone number is (571) 272-2917. The examiner can normally be reached on Monday through Friday 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) (http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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Tara L Garvey
Examiner
Art Unit 1636

TLG

JAMES KETTER
PRIMARY EXAMINER